UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

In re APELLIS PHARMACEUTICALS, INC. SECURITIES LITIGATION	)	No. 1:24-cv-11470-JEK

MEMORANDUM AND ORDER ON DEFENDANTS' MOTION TO DISMISS

KOBICK, J.

In this putative class action, the plaintiffs allege that defendants Apellis Pharmaceuticals, Inc. and its Chief Executive Officer, Dr. Cedric Francois, made materially misleading omissions during two phase three clinical trials of its drug, SYFOVRE, in violation of sections 10(b) and 20(a) of the Securities Exchange Act of 1934 and Securities and Exchange Commission ("SEC") Rule 10b-5. Apellis is a biopharmaceutical company that developed SYFOVRE to treat geographic atrophy, an advanced form of age-related macular degeneration that can cause blindness. The lead plaintiffs and putative class members purchased Apellis's stock between January 28, 2021 and July 28, 2023. They principally challenge the defendants' statements that there were no reported cases of retinal vasculitis—a severe inflammation of retinal blood vessels—during the clinical trials. Conceding that those statements were accurate, the plaintiffs contend that the statements were nonetheless fraudulent because the defendants simultaneously omitted material information about how frequently Apellis was testing for retinal vasculitis and that its clinical trial protocol was allegedly inadequate to detect the condition.

Pending before the Court is the defendants' motion to dismiss the amended complaint with prejudice and without leave to amend. The defendants contend that the plaintiffs do not adequately allege that the specified omissions were materially misleading to investors under the heightened pleading standards of Federal Rule of Civil Procedure 9(b) and the Private Securities Litigation

Reform Act of 1995, and that the plaintiffs' allegations do not give rise to a strong inference of scienter. Agreeing with these arguments, the Court will grant the defendants' motion.

BACKGROUND

I. Factual Background.

The Court recounts the facts based on the allegations in the amended complaint and "the content of documents . . . sufficiently referenced" therein. *Bazinet v. Beth Israel Lahey Health, Inc.*, 113 F.4th 9, 15 (1st Cir. 2024).

Lead plaintiffs Ray Peleckas and Michigan Laborers' Pension Fund, as well as putative class members, purchased common stock of Apellis between January 28, 2021 and July 28, 2023 (the "Class Period"). ECF 54, ¶¶ 1, 22. Dr. Francois is a co-founder of Apellis and has served as a member of its board of directors and its President and Chief Executive Officer since its inception. *Id.* ¶ 25. Apellis is a commercial-stage biopharmaceutical company that, as relevant here, developed its "lead product candidate" of pegcetacoplan—now commercially called SYFOVRE—to treat geographic atrophy through an injection directly into the eye. *Id.* ¶¶ 3, 23, 33, 36, 41. An advanced form of age-related macular degeneration, geographic atrophy affects the central portion of the retina and can lead to blindness in people aged sixty or older. *Id.* ¶ 34. Injections of pegcetacoplan can slow the progression of macular degeneration by targeting certain complement proteins to enhance cell survival and reduce vascular loss, but they do not cure the disease. *Id.* ¶¶ 4-5, 37.

Pegcetacoplan has potential side effects. *Id.* ¶ 41. Three are relevant here: (1) retinal or intraocular inflammation, (2) ischemic optic neuropathy, and (3) retinal vasculitis. *Id.* Retinal or intraocular inflammation involves an over-activation of the immune system in the eye that, if left untreated, can evolve into retinal vasculitis. *Id.* ¶¶ 42, 49. Ischemic optic neuropathy involves

impaired blood flow to the area near the head of the optic nerve. *Id.* ¶ 44. Retinal vasculitis is a more severe form of inflammation of retinal blood vessels that, in its worst form, can cause complete vision loss. *Id.* ¶¶ 43, 46, 49. Doctors commonly use a test known as a fluorescein angiogram to look for retinal vasculitis. *Id.* ¶ 48.

On January 28, 2021, at the start of the Class Period, Apellis was in the process of conducting two phase three clinical trials of pegcetacoplan. *Id.* ¶ 3. Those trials were named OAKS and DERBY. *Id.* Apellis had enrolled over a thousand patients aged sixty and older with geographic atrophy secondary to age-related macular degeneration in these two-year studies, and it randomly provided the study participants with either pegcetacoplan or a sham treatment. *Id.* ¶¶ 40, 59; ECF 82-7, at 3. On January 28, 2021, Apellis stated during a Virtual Investor Event that its prior phase two clinical trial "met [its] primary endpoint, reducing [geographic atrophy] lesion growth," and that "[t]op-line results [were] expected [in] Q3 2021" from the phase three studies. ECF 54, ¶ 76. Dr. Francois also characterized the then-forthcoming results from the phase three studies as "a seminal event" for Apellis. *Id.* ¶¶ 3, 159. The effects of pegcetacoplan on patients with geographic atrophy, including whether any trial participants experienced retinal vasculitis, mattered to investors because the presence of retinal vasculitis could impair market acceptance of the drug. *Id.* ¶ 47.

On September 9, 2021, at the one-year mark of the OAKS and DERBY trials, Apellis announced its top-line results, which showed a 16% to 22% reduction in geographic atrophy lesion size. *Id.* ¶¶ 4, 77; ECF 82-7, at 2. This was slightly less than the 20% to 30% reduction that Dr. Francois had described in October 2020 as "clinically meaningful." ECF 54, ¶ 4. A Credit Suisse analyst that day portrayed these results as "at the low end of what physicians . . . highlighted as meaningful." *Id.* Apellis also represented that "[n]o events of retinal vasculitis or retinal vein

occlusion were observed," and that while thirteen cases of intraocular inflammation were reported, "[t]here were no clinically relevant changes in vision for patients who developed . . . intraocular inflammation." *Id.* ¶ 77; ECF 82-7, at 3.

Over the next twelve months, Apellis continued to make similar representations about the OAKS and DERBY studies. In presentations published on October 11 and November 12, 2021, Apellis stated that "[t]here were no cases of vasculitis or occlusive vasculitis." ECF 54, ¶¶ 6, 78, 82; ECF 82-8, at 8; ECF 82-9, at 18. In public statements and reports in November 2021, February 2022, and March 2022, Apellis again noted that "[n]o events of retinal vasculitis or retinal vein occlusion were observed" in either trial. ECF 54, ¶¶ 80, 84, 86; ECF 82-5, at 8; ECF 82-10, at 3. Apellis's November 8, 2021 10-Q quarterly report and its February 28, 2022 Form 10-K annual report represented that "[t]here were no clinically relevant changes in vision for patients who developed . . . intraocular inflammation." ECF 54, ¶¶ 80, 84; ECF 82-2, at 13; ECF 82-3, at 12. The March 16, 2022 press release also stated that "the rate of intraocular inflammation was 0.23% per injection," which was "generally in line with [the rates] reported in studies of other intravitreal therapies." ECF 82-10, at 3; ECF 54, ¶ 65. In presentations published in May and July 2022, Apellis explained that while no cases "of retinitis or vasculitis (occlusive or non-occlusive)" were reported in the OAKS or DERBY trials, there were instances of intraocular inflammation. ECF 54, ¶¶ 88, 90; ECF 82-11, at 24; ECF 82-12, at 13. Apellis's Form 10-Q quarterly report filed with the SEC in August 2022 reiterated that, through June 2022, "[n]o events of retinal vasculitis or retinal vein occlusion were observed" in the OAKS or DERBY trials. ECF 54, ¶ 92.

Based on data from the two completed trials, Apellis announced, in late August 2022, that "[n]o events of occlusive vasculitis or retinitis were observed over 24 months." *Id.* ¶ 94; ECF 82-14, at 6. The data also revealed that patients who received pegcetacoplan were ten to twenty times

more likely than those in the sham arm to develop retinal inflammation. ECF 54, ¶ 59. It further showed that some patients treated with pegcetacoplan, unlike those who received the sham treatment, reported ischemic optic neuropathy. *Id.* ¶ 62. Around the same time, Dr. Francois said on a conference call that the DERBY and OAKS results continued to show "a favorable safety profile in line with what [Apellis] saw at 12 and 18 months." *Id.* ¶ 96. Apellis and Dr. Francois stated again in November 2022 that there were "[n]o reports of occlusive or nonocclusive retinitis or vasculitis" in either clinical trial. *Id.* ¶ 98; ECF 82-15, at 8; *see* ECF 54, ¶ 100 (Dr. Francois stating at a conference that it is "correct" that "to date, no vasculitis or retinitis" had been observed).

On February 17, 2023, the Food and Drug Administration ("FDA") approved Apellis's pegcetacoplan injections under the name SYFOVRE to treat geographic atrophy in the United States. ECF 54, ¶¶ 38, 102. During a conference call that same day, Apellis highlighted that "[n]o events of occlusive or non-occlusive vasculitis or retinitis were observed" in the DERBY and OAKS trials. *Id.* ¶ 104. Apellis's February 21, 2023 Form 10-K annual report stated the same. *Id.* ¶ 106; ECF 82-4, at 13.

The plaintiffs contend that Apellis's claims that there were no observed cases of retinal vasculitis or retinal vein occlusion in the OAKS and DERBY trials were materially misleading. This is so, the plaintiffs maintain, because Apellis omitted the fact that the defined protocol for OAKS and DERBY did not require it to timely obtain fluorescein angiography, the test commonly used to detect vasculitis, for patients who left the trials early or who developed intraocular inflammation or ischemic optic neuropathy. ECF 54, ¶¶ 7, 48, 64. The protocol for the trials, dated August 12, 2020, was approved by the FDA and was made publicly available on the ClinicalTrials.gov website during the Class Period. ECF 82-17; ECF 82, ¶ 17; ECF 81, at 11 n.11;

ECF 83, at 13. Under this protocol, participants in the trials were given a fluorescein angiogram at the outset of OAKS and DERBY, at twelve and twenty-four months into the trials, and within thirty days of a participant's early termination from the trials. ECF 82-17, at 16, 36, 43-46; ECF 81, at 11. According to the plaintiffs and their expert, Dr. Demetrios Vavvas,[1] the protocol was inadequate because had Apellis promptly performed angiograms on participants with inflammation or ischemic optic neuropathy, it could have determined if they also had retinal vasculitis. ECF 54, ¶¶ 7, 60, 63.

On July 15, 2023, five months after the FDA approved SYFOVRE, the American Society of Retina Specialists ("ASRS") reported six incidents of retinal vasculitis in patients treated with SYFOVRE. *Id.* ¶¶ 9, 108. Following that news, Apellis's stock fell approximately 38%, from $84.50 per share on July 14, 2023 to $52.46 per share on July 17, 2023. *Id.* ¶¶ 10, 109. Apellis announced that it was investigating these incidents on July 17, 2023. *Id.* ¶¶ 11, 110. On July 29, 2023, beyond the Class Period, Apellis confirmed another case of retinal vasculitis. *Id.* ¶¶ 15, 114; ECF 82-18, at 1-2. In response, Apellis's stock declined further to close at $25.75 per share on July 31, 2023. ECF 54, ¶¶ 16, 115. This amounts to a decline of nearly 70% from a high of $84.50 per share and constitutes a nearly $7 billion loss in market capitalization. *Id.* ¶ 17.

In November 2023, Apellis updated SYFOVRE's label to include a warning for retinal vasculitis. *Id.* ¶ 116. On December 21, 2023, the ASRS issued an additional report finding that while "'[t]here were no reported cases of retinal vasculitis or occlusive retinal vasculopathy in the clinical trials'" for SYFOVRE, "'there was no defined protocol in these studies to obtain angiography in cases of intraocular inflammation.'" *Id.* ¶ 117 (quoting ECF 97, Witkin et al.,

[1] Dr. Vavvas is the Solman and Libe Friedman Professor of Ophthalmology, and Co-Director of the Ocular Regenerative Medicine Institute, at Harvard Medical School. ECF 54, ¶ 60. He also serves as the Director of the Retina Service at Massachusetts Eye and Ear. *Id.*

Retinal Vasculitis After Intravitreal Pegcetacoplan: Report from the ASRS Research and Safety in Therapeutics (ReST) Committee, 8 J. VITREORETINAL DISEASES 9, 15 (2023)).

II. Procedural History.

The initial complaint in this matter was filed in the District of Delaware in August 2023. ECF 1. Ray Peleckas and Michigan Laborers' Pension Fund were appointed as lead plaintiffs in October 2023. ECF 45. In February 2024, the plaintiffs filed an amended complaint, alleging that Apellis and Dr. Francois violated section 10(b) of the Securities Exchange Act of 1934 and Rule 10b-5 (Count I); and that Dr. Francois violated section 20(a) of the Securities Exchange Act of 1934 (Count II). ECF 54, ¶¶ 180-92. Three months later, in May 2024, the District Court in Delaware transferred the case to this Court. ECF 68. In June 2024, following transfer, the defendants moved to dismiss the complaint with prejudice and without leave to amend. ECF 80. After the plaintiffs opposed that motion and the defendants filed their reply brief, the Court held a hearing and took the matter under advisement. ECF 83, 89, 97.

DISCUSSION

The plaintiffs allege violations of federal securities laws—namely, sections 10(b) and 20(a) of the Securities Exchange Act of 1934, 15 U.S.C. §§ 78j(b), 78t(a), and Rule 10b-5 promulgated thereunder, 17 C.F.R. § 240.10b-5. ECF 54, ¶¶ 18, 180-92. Section 10(b) makes it unlawful "[t]o use or employ, in connection with the purchase or sale of any security . . . any manipulative or deceptive device or contrivance in contravention of such rules and regulations as the [SEC] may prescribe as necessary or appropriate in the public interest or for the protection of investors." 15 U.S.C. § 78j(b). Rule 10b-5, in turn and as applicable here, makes it unlawful "[t]o make any untrue statement of material fact or to omit to state a material fact necessary in order to make the statements made, in light of the circumstances under which they were made, not misleading." 17

C.F.R. § 240.10b-5(b). "Rule 10b-5 'is coextensive with the coverage of [section] 10(b).'" *Ponsa-Rabell v. Santander Sec. LLC*, 35 F.4th 26, 32 (1st Cir. 2022) (quoting *S.E.C. v. Zandford*, 535 U.S. 813, 816 n.1 (2002)).

"For a complaint to state a claim for securities fraud under section 10(b) and Rule 10b-5, it must plead six elements: (1) a material misrepresentation or omission; (2) scienter, or a wrongful state of mind; (3) a connection with the purchase or sale of security; (4) reliance; (5) economic loss; and (6) loss causation." *ACA Fin. Guar. Corp. v. Advest, Inc.*, 512 F.3d 46, 58 (1st Cir. 2008); *accord Zhou v. Desktop Metal, Inc.*, 120 F.4th 278, 287 (1st Cir. 2024). A claim under section 20(a), which "imposes joint and several liability on persons in control of entities that violate the securities laws," is "derivative of an underlying violation of the securities laws." *Fire & Police Pension Ass'n of Colorado v. Abiomed, Inc.*, 778 F.3d 228, 246 (1st Cir. 2015). Where there is "no underlying 10b-5 violation," the "section 20(a) claim must fail." *ACA Fin. Guar. Corp.*, 512 F.3d at 68.

I. Pleading Standard Under the Private Securities Litigation Reform Act and Federal Rule of Civil Procedure 9(b).

To survive a motion to dismiss federal securities fraud claims, the amended complaint must adhere to the heightened pleading requirements of Federal Rule of Civil Procedure 9(b) and the Private Securities Litigation Reform Act of 1995 ("PSLRA"), 15 U.S.C. § 78u-4. *Zhou*, 120 F.4th at 287. "As with any motion to dismiss under Rule 12(b)(6)," the Court must "'accept well-pleaded factual allegations in [the amended] complaint as true and view all reasonable inferences in [the plaintiffs'] favor.'" *Id.* (quoting *ACA Fin. Guar. Corp.*, 512 F.3d at 58). The Court may, however, supplement its review of the factual allegations in the amended complaint with materials filed in connection with the motion to dismiss, to the extent that they "include 'documents the authenticity of which are not disputed by the parties,' 'official public records,' and 'documents sufficiently

referred to in the complaint.'" *Constr. Indus. & Laborers Joint Pension Tr. v. Carbonite, Inc.*, 22 F.4th 1, 4 (1st Cir. 2021) (quoting *Mehta v. Ocular Therapeutix, Inc.*, 955 F.3d 194, 198 (1st Cir. 2020)). The amended complaint "must contain sufficient factual matter, accepted as true, to 'state a claim for relief that is plausible on its face.'" *Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009) (quoting *Bell Atlantic Corporation v. Twombly*, 550 U.S. 544, 570 (2007)). In addition, under Rule 9(b), the plaintiffs "'must state with particularity the circumstances constituting fraud' in the pleading, but '[m]alice, intent, knowledge, and other conditions of a person's mind may be alleged generally.'" *Hill v. Gozani*, 638 F.3d 40, 55 (1st Cir. 2011) (quoting Fed. R. Civ. P. 9(b)).

The PSLRA goes further than Rule 9(b) with respect to the pleading requirements for the first two elements of claims under section 10(b) and Rule 10b-5. *Id.* at 55. To plead a material misrepresentation or omission (the first element) under the PSLRA, the complaint must "specify each statement alleged to have been misleading, the reason or reasons why the statement is misleading, and, if an allegation regarding the statement or omission is made on information and belief, the complaint shall state with particularity all facts on which that belief is formed." 15 U.S.C. § 78u-4(b)(1). To plead scienter (the second element), the complaint must "with respect to each act or omission . . . state with particularity facts giving rise to a strong inference that the defendant[s] acted with the required state of mind." *Id.* § 78u-4(b)(2)(A). "While under Rule 12(b)(6) all inferences must be drawn in plaintiffs' favor, inferences of scienter do not survive if they are merely reasonable, as is true when pleadings for other causes of action are tested by motion to dismiss under Rule 12(b)(6)." *ACA Fin. Guar. Corp.*, 512 F.3d at 59 (quotation marks omitted). The Court "must engage in a comparative evaluation; it must consider, not only inferences [of scienter] urged by the plaintiff[s] . . . but also competing inferences rationally drawn from the facts alleged." *Tellabs, Inc. v. Makor Issues & Rights, Ltd.*, 551 U.S. 308, 314 (2007). If there are

"equally strong inferences for and against scienter," the Court must "award the draw to the plaintiff[s]." *ACA Fin. Guar. Corp.*, 512 F.3d at 59.

II. The Plaintiffs' Allegations.

The amended complaint alleges material omissions rather than material misrepresentations. The plaintiffs do not contend that the defendants inaccurately reported that there were no instances of retinal vasculitis in the OAKS and DERBY trials. Nor do the plaintiffs allege that the defendants described their trial protocol incorrectly, failed to test for retinal vasculitis at all, or improperly manipulated the protocol during those studies to decrease the likelihood of observing cases of retinal vasculitis. Rather, the plaintiffs claim that the defendants' statements about the absence of retinal vasculitis in OAKS or DERBY participants misled investors because the defendants did not at the same time disclose how frequently Apellis was testing for retinal vasculitis or the alleged inadequacy of the protocol Apellis used to detect the condition.[2]

A. Material Omissions.

To establish the first element of their section 10(b) and Rule 10b-5 claim—a material omission—the plaintiffs "'must show that [the] defendants . . . omitted to state a material fact necessary to make a statement not misleading.'" *Ponsa-Rabell*, 35 F.4th at 32-33 (quoting *Ganem v. InVivo Therapeutics Holdings Corp.*, 845 F.3d 447, 454 (1st Cir. 2017)). "'Information is material if a reasonable investor would have viewed it as having significantly altered the total mix of information made available.'" *Id.* at 33 (quoting *Mississippi Pub. Emps.' Ret. Sys. v. Bos. Sci. Corp.*, 523 F.3d 75, 85 (1st Cir. 2008)). "[W]hether a statement is 'misleading' depends on the

[2] The amended complaint alludes to other theories about why the defendants' statements were false or misleading, but the plaintiffs have waived those theories by not advancing them in their opposition after the defendants briefed them in their motion to dismiss. *See Zhou*, 120 F.4th at 289-91 (holding that the plaintiff did not preserve her scheme liability claim because she did not address it in her opposition to the motion to dismiss).

perspective of a reasonable investor." *Omnicare, Inc. v. Laborers Dist. Council Constr. Indus. Pension Fund*, 575 U.S. 175, 186 (2015). Since "section 10(b) and Rule 10b-5 'do not create an affirmative duty to disclose any and all material information,'" a material omission "is actionable only if it 'renders affirmative statements made misleading.'" *Zhou*, 120 F.4th at 292 (citations omitted). Such "half-truths" are prohibited because they "pain[t] a materially false picture in what they say because of what they omit." *Sec. & Exch. Comm'n v. Johnston*, 986 F.3d 63, 72 (1st Cir. 2021); *see Macquarie Infrastructure Corp. v. Moab Partners, L. P.*, 601 U.S. 257, 258 (2024) ("Half-truths . . . are 'representations that state the truth only so far as it goes, while omitting critical qualifying information.'" (quoting *Universal Health Servs., Inc. v. United States*, 579 U.S. 176, 188 (2016))). The Court must "evaluate [t]he immediate context of each statement—namely, the balance of what was said on the particular occasion, and the immediate circumstances in which the particular statement was made." *Zhou*, 120 F.4th at 293 (quotation marks omitted).

The plaintiffs claim that the defendants' statements concerning the absence of retinal vasculitis in the DERBY and OAKS trials are actionable half-truths because they omitted (1) how frequently Apellis was using fluorescein angiography to test for retinal vasculitis, and (2) that their protocol was allegedly inadequate to detect that condition. ECF 83, at 2, 9-10.[3] The first alleged omission, concerning the frequency of angiography testing in the trial participants, was not, as a matter of law, misleading because the frequency of testing under the trial protocol was

[3] The plaintiffs also challenge Apellis's January 28, 2021 statements that the phase two trial "met [its] primary endpoint, reducing [geographic atrophy] lesion growth," and that "the DERBY and OAKS trials would improve upon the robust [phase two] trial with [t]op-line results expected Q3 2021." ECF 54, ¶ 76. Even though these statements, unlike the other challenged statements, do not mention vasculitis, the plaintiffs contend they are likewise "misleading in light of [d]efendants' failure to disclose the inadequacy of their testing protocol." ECF 83, at 14 n.14. The Court considers these statements, as well as the others identified in the amended complaint, in its analysis. *See id.* ¶¶ 76-78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106.

"'information [already] made available'" to investors well before the defendants made the challenged statements during the Class Period. *Basic Inc. v. Levinson*, 485 U.S. 224, 232 (1988) (quoting *TSC Indus., Inc. v. Northway, Inc.*, 426 U.S. 438, 449 (1976)). The parties agree that the protocol's fifth amended version, dated August 12, 2020, was publicly available on the ClinicalTrials.gov website during the Class Period. *See* ECF 82-17 (protocol); ECF 81, at 11 n.11; ECF 83, at 5 n.4; ECF 99, at 39-41. The governing regulations require companies like Apellis to submit their clinical trial protocols, including any amendments, to that website, run by the National Institutes of Health ("NIH"), and the NIH Director must, in turn, post that information on ClinicalTrials.gov within 30 days of the date of submission. *See* 42 C.F.R. §§ 11.48(a)(5), 11.52; *Abely v. Aeterna Zentaris Inc.*, No. 12-cv-4711-PKC, 2013 WL 2399869, at *13 & n.7 (S.D.N.Y. May 29, 2013) ("Federal law requires the publication and filing of [protocols]."). Thus, the protocol's fifth iteration, submitted in August 2020, was available online to investors throughout the Class Period.

The protocol, which is incorporated by reference into the amended complaint, disclosed that participants were given a fluorescein angiogram at the outset of the OAKS and DERBY trials, at approximately twelve and twenty-four months into the trials, and within thirty days of a patient's early termination from the trials. ECF 82-17, at 16, 36, 43-46, 72-83; *see* ECF 81, at 11. In the plaintiffs' view, the defendants' repeated representations that there were no cases of retinal vasculitis in the OAKS and DERBY trials were materially misleading because they omitted how frequently angiography was being conducted, including the fact that the protocol did not require angiography immediately upon the detection of retinal inflammation or ischemic neuropathy. But "it is not a material omission to fail to point out information of which the market is already aware." *Thant v. Karyopharm Therapeutics Inc.*, 43 F.4th 214, 222 (1st Cir. 2022) (quotation marks

omitted). The defendants were "not under any duty to repeat" when angiography was required because that information was "readily accessible to" the plaintiffs. *Ponsa-Rabell*, 35 F.4th at 35. Reasonable investors were on notice of the protocol and would not, therefore, have been misled by the defendants' statements into believing that more testing was occurring than what was provided for in the public protocol. *See Omnicare*, 575 U.S. at 186; ECF 83, at 13 (plaintiffs conceding "the public nature of the protocol").

Public presentations to investors during the Class Period, which are similarly incorporated by reference into the amended complaint, also repeatedly disclosed when fluorescein angiography—often abbreviated "FA"—was conducted. Apellis's October 11, 2021 presentation, for example, represented that "FA was captured per protocol at Screening and Month 12." ECF 82-8, at 16-17; *see* ECF 54, ¶ 78. Apellis expressed the same in its November 12, 2021 presentation. ECF 82-9, at 22; *see* ECF 54, ¶ 82. Apellis's May 2, 2022 presentation noted that "the next protocol-specified FA is at Month 24." ECF 82-11, at 23; *see* ECF 54, ¶ 88. These presentations further placed investors on notice of the protocol and the frequency with which fluorescein angiography was performed under it. Reasonable investors would not, accordingly, have inferred from the defendants' statements about the absence of retinal vasculitis that more testing was being done. Instead, they would have understood that Apellis was testing for vasculitis as the protocol prescribed. *See Fernandes v. Centessa Pharms. PLC*, No. 22-cv-8805-GHW, 2024 WL 3638254, at *18 (S.D.N.Y. Aug. 2, 2024) (finding no actionable omissions where "much of the 'critical context' that Plaintiffs alleged was missing from the Registration Statement was, in fact, in it" and "Plaintiffs' remaining [in-hindsight] critiques merely disagree with the underlying studies' designs"); *Gregory v. ProNAi Therapeutics Inc.*, 297 F. Supp. 3d 372, 411 (S.D.N.Y. 2018) (dismissing nondisclosure claim where defendant publicly "disclosed the protocol

amendments on ClinicalTrials.gov"), *aff'd*, 757 F. App'x 35 (2d Cir. 2018). The defendants, in turn, had no obligation to repeat the protocol's contents when making accurate statements about the absence of retinal vasculitis in the clinical trials.

The plaintiffs' related theory—that the protocol would not reliably detect cases of retinal vasculitis—merely involves a scientific disagreement over the proper frequency for conducting fluorescein angiography. In the plaintiffs' telling, the defendants failed to "adequately tes[t]" for retinal vasculitis with that method of assessment. ECF 83, at 10. To support this theory, the plaintiffs rely on their expert, Dr. Vavvas, who opines that Apellis should have known, based on the presence of inflammation and ischemic optic neuropathy in some trial participants, and based on the higher rate of participant drop-outs in the pegcetacoplan treatment group than the sham treatment group, that a risk of retinal vasculitis existed. ECF 54, ¶¶ 61-62, 73-75. The plaintiffs contend that the defendants did not make "the type of inquiry that a reasonable investor would expect given the circumstances," because such an investor would infer that Apellis would have obtained fluorescein angiography immediately for patients who left the clinical trials or more promptly for those who experienced retinal inflammation or ischemic neuropathy. *Carbonite*, 22 F.4th at 7 (citing *Omnicare*, 575 U.S. at 188-89).

Such a challenge to the methodology of Apellis's trials is not sufficient to state a misleading omission claim. As this Court explained in *Kader v. Sarepta Therapeutics, Inc.*, a "criticism of drug study methodology is insufficient to state a claim for securities fraud, particularly where there is no showing of an intent to deceive or improper manipulation of results." No. 14-cv-14318-ADB, 2017 WL 72396, at *7 (D. Mass. Jan. 6, 2017), *aff'd*, 887 F.3d 48 (1st Cir. 2018); *see also, e.g.*, *In re Rigel Pharms., Inc. Sec. Litig.*, 697 F.3d 869, 879 (9th Cir. 2012) (holding that the "Plaintiff did not adequately plead falsity" because it "criticize[d] only the statistical methodology employed

by Defendants"); *Abely*, 2013 WL 2399869, at *7 ("[I]n scrutinizing a section 10(b) claim, a court does not judge the methodology of a drug trial, but whether a defendant's statements about that study were false and misleading." (citing *Kleinman v. Elan Corp., plc*, 706 F.3d 145, 154-55 (2d Cir. 2013))). That is especially so here, given that the FDA approved Apellis's protocol for testing for retinal vasculitis and a reasonable investor would have known about that protocol. The plaintiffs speculate that reasonable investors would have believed, based on the defendants' statements about the absence of observed cases of retinal vasculitis, that Apellis was performing the additional testing suggested by Dr. Vavvas. To the contrary, a reasonable investor would have believed that Apellis was conducting fluorescein angiography at the frequency or upon the occurrences specified in the FDA-approved protocol. *See Lungu v. Antares Pharma Inc.*, No. 21-1624, 2022 WL 212309, at *6 (3d Cir. Jan. 25, 2022) ("Given that the FDA approved the methods and procedures employed in the second clinical study, no reasonable investor would be concerned with patient enrollment data with which the FDA did not take issue."); *Tongue v. Sanofi*, 816 F.3d 199, 213 (2d Cir. 2016) ("Especially where a complex financial instrument whose value is tied to FDA approval is involved, investors may be expected to keep themselves apprised of the FDA's public positions on testing methodology."). Where, as here, "a company accurately reports the results of a scientific study, it is under no obligation to second-guess the methodology of that study." *Emps.' Ret. Sys. of the City of Baton Rouge & Par. of E. Baton Rouge v. MacroGenics, Inc.*, 61 F.4th 369, 385 (4th Cir. 2023) (quotation marks omitted); *see In re Sepracor, Inc. Sec. Litig.*, 308 F. Supp. 2d 20, 36 (D. Mass. 2004) ("The securities laws do not impose a duty to conduct 'good science.'" (quotation marks omitted)).

The plaintiffs further point to a November 2020 article and a December 2023 report by the ASRS in support of their theory. ECF 54, ¶¶ 117, 153-54. Those sources do not convert the

plaintiffs' scientific disagreement with the defendants over methodology into an actionable securities fraud claim. The article—published in November 2020 by, among others, the lead investigator for DERBY, Dr. Jeffrey Heier—stated that "injections should cease" and angiography "should be performed" "[i]f inflammation is detected" in patients treated with a different drug for age-related macular degeneration, named Beovu (brolucizumab). *Id.* ¶¶ 55, 153-54. The article does not, however, address SYFOVRE (pegcetacoplan); it merely recommends angiography if patients experience inflammation when treated with Beovu. ECF 89, at 5-6 & n.7 (citing Monés, et al., *Risk of Inflammation, Retinal Vasculitis, and Retinal Occlusion-Related Events with Brolucizumab*, 128 AM. ACAD. OPHTHALMOLOGY 1050 (Nov. 2020)). The ASRS's December 21, 2023 report found that while "[t]here were no reported cases of retinal vasculitis or occlusive retinal vasculopathy in the clinical trials" for SYFOVRE, "there was no defined protocol in these studies to obtain angiography in cases of intraocular inflammation." ECF 97, at 15. Neither the defendants nor the publicly available protocol disclosed anything to the contrary. While the plaintiffs, Dr. Vavvas, and allegedly the ASRS may disagree with the defendants and the FDA about whether more frequent fluorescein angiograms would have been proper for instances of intraocular inflammation, this "legitimate disagreement over scientific [methodology] does not give rise to a securities fraud claim." *Shash v. Biogen, Inc.*, 84 F.4th 1, 17 (1st Cir. 2023) (quotation marks omitted); *see Nathenson v. Zonagen Inc.*, 267 F.3d 400, 420 (5th Cir. 2001) (observing that "[m]edical researchers may well differ with respect to what constitutes acceptable testing procedures" in affirming dismissal of fraud allegations concerning phase three trials). Because Apellis employed the methodology prescribed for testing for retinal vasculitis by the publicly available, FDA-approved protocol, the plaintiffs do not plausibly allege that the defendants' statements about the absence of retinal vasculitis contained materially misleading omissions.

B. Scienter.

The amended complaint must also be dismissed for the independent reason that the plaintiffs fail to adequately plead scienter. Under the PSLRA, to plead scienter, the amended complaint must "with respect to each act or omission . . . state with particularity facts giving rise to a *strong* inference that the defendant[s] acted with the required state of mind." 15 U.S.C. § 78u-4(b)(2)(A) (emphasis added). "Scienter is 'a mental state embracing intent to deceive, manipulate, or defraud.'" *Shash*, 84 F.4th at 13 (quoting *Mehta*, 955 F.3d at 206). "To establish scienter, plaintiff[s] must 'show either that the defendants consciously intended to defraud, or that they acted with a high degree of recklessness.'" *Carbonite*, 22 F.4th at 8 (quoting *Kader*, 887 F.3d at 57). "In this context, recklessness requires more than 'simple, or even inexcusable, negligence'; rather, recklessness is 'a highly unreasonable omission' amounting to 'an extreme departure from the standards of ordinary care, and which presents a danger of misleading buyers and sellers that is either known to the defendant[s] or is so obvious that the actor must have been aware of it.'" *Shash*, 84 F.4th at 13 (quoting *Mehta*, 955 F.3d at 206). "An inference of scienter is 'strong' if 'a reasonable person would deem [it] cogent and at least as compelling as any opposing inference one could draw from the facts alleged.'" *Fire & Police Pension Ass'n of Colorado*, 778 F.3d at 240-41 (quoting *Tellabs*, 551 U.S. at 324).

Often in cases where the scienter pleading standard is satisfied, the complaint "contains clear allegations of admissions, internal records or witnessed discussions suggesting that at the time they made the statements claimed to be misleading, the defendant officers were aware that they were withholding vital information or at least were warned by others that this was so." *In re Bos. Sci. Corp. Sec. Litig.*, 686 F.3d 21, 31 (1st Cir. 2012). "[T]he fact that a defendant knowingly made a false statement is 'classic evidence' of scienter." *ACA Fin. Guar. Corp.*, 512 F.3d at 65

(quoting *Aldridge v. A.T. Cross Corp.*, 284 F.3d 72, 83 (1st Cir. 2002)). "[W]here a complaint is devoid of any direct-evidence allegations, the indirect-evidence allegations in the complaint will need to do more work to carry the burden of raising a strong inference of scienter on their own." *Shash*, 84 F.4th at 16 (quotation marks omitted).

The amended complaint is devoid of allegations resembling direct evidence of scienter. Instead, relying on *Carbonite*, the plaintiffs contend that the defendants acted with a high degree of recklessness because they were "paying close attention" to SYFOVRE, as Apellis's lead product candidate, such that their statements about the absence of retinal vasculitis in the OAKS and DERBY trials should have "invited further investigation." 22 F.4th at 9-10 (quotation marks omitted). In *Carbonite*, the First Circuit explained that "'the importance of a particular item to a defendant can support an inference that the defendant is paying close attention to that item,' if 'that close attention would have revealed an incongruity so glaring as to make the need for further inquiry obvious.'" *Id.* at 9 (quoting *Loc. No. 8 IBEW Ret. Plan & Tr. v. Vertex Pharms., Inc.*, 838 F.3d 76, 82 (1st Cir. 2016)). To support an inference of scienter, however, the amended complaint "must allege particular facts strongly suggesting that that attention exposed [the defendants] to information that either rendered their public statements false or necessarily invited further investigation." *Id.* at 9-10. The defendants in *Carbonite* had publicly asserted that their important product was "super strong," but, at the time of their statement, the product had never once worked and employees with knowledge of the product had reported internally that it was not ready for market. *Id.* at 10. Those alleged facts, the First Circuit reasoned, dispelled "the possibility that [the company's] management was somehow in the dark about [the product's] true status" at the time of their remarks, thus supporting an inference that the defendants were at least highly reckless. *Id.*

Here, in contrast, the amended complaint does not allege that, at the time of the relevant statements, Apellis, Dr. Francois, or any Apellis employee knew or reported that there were cases of retinal vasculitis in the OAKS and DERBY trials, or that the FDA-approved protocol insufficiently tested for that condition. Nor does the amended complaint allege that the defendants or any Apellis staff member, during the Class Period, shared the view of the plaintiffs and their expert, Dr. Vavvas, that the protocol tested for retinal vasculitis too infrequently. The article by DERBY's lead investigator, Dr. Heier, which recommended angiography in patients who experienced inflammation, does not give rise to a strong inference of scienter because it concerned a different drug. ECF 54, ¶ 154. The plaintiffs also notably do not allege that Dr. Heier raised any concerns about the protocol for OAKS and DERBY. *See Auto. Indus. Pension Tr. Fund v. Textron Inc.*, 682 F.3d 34, 39 (1st Cir. 2012) (holding that "the complaint fail[ed] adequately to allege scienter" where "warnings by subordinates or expressions of concern by executives [were] notably absent"). Accordingly, notwithstanding the importance of SYFOVRE as a lead product candidate at Apellis, the facts alleged do not support an inference that the defendants knew, or were reckless in not knowing, that their statements about the absence of retinal vasculitis in the clinical trials were misleading. *See Metzler Asset Mgmt. GMBH v. Kingsley*, 928 F.3d 151, 165 (1st Cir. 2019) (concluding that the plaintiffs did not establish scienter on a "core operations" theory where they "fail[ed] to identify any allegations in the complaint that show[ed] that anyone in the company had knowledge regarding the drug's safety profile and sales that contradicted the company's public representations").

As additional evidence that the defendants should have inquired further to assess whether trial participants had retinal vasculitis, the plaintiffs point to increased dropout rates and greater instances of inflammation and neuropathy, which are potential symptoms of vasculitis, in the

pegcetacoplan treatment arm than the sham arm. ECF 54, ¶¶ 59, 61-62. But absent any allegation that the defendants were aware that the defined protocol was inadequate, the defendants' failure to identify deficiencies in the protocol for angiography when reporting no cases of vasculitis in the OAKS and DERBY trials does not support an inference of scienter. *See Shash*, 84 F.4th at 19 (finding scienter lacking where "[t]he complaint contain[ed] no allegation that Defendants knew the subgroup data undermined their efficacy statements"); *Angelos v. Tokai Pharms., Inc.*, 494 F. Supp. 3d 39, 58 (D. Mass. 2020) (dismissing section 10(b) claims in part because there were "no allegations of any internal reports or communications indicating that defendants knew of problems with the Phase 3 trial when the allegedly misleading statements were made").[4]

Finally, to demonstrate scienter, the plaintiffs advance a propensity-to-lie theory that relies on actions taken by the defendants after the allegedly misleading statements were made and after the Class Period. They assert, for example, that the defendants sought to mislead investors about the cause of retinal vasculitis after the ASRS reported six such cases in patients treated with SYFOVRE by blaming those cases on faulty needles used for injections, misdiagnoses, and manufacturing issues, but not the drug itself. ECF 54, ¶¶ 118-31. They also allege that the defendants manipulated the data by, among other things, describing the incidence of retinal

[4] Dr. Vavvas's assessment that "management/CEO/the Company had to have known there was a real risk of vasculitis, which should have been disclosed," also lacks force because Apellis repeatedly disclosed to investors that adverse events not observed in the OAKS and DERBY trials, such as vasculitis, could materialize after FDA approval of its pegcetacoplan treatment. ECF 54, ¶ 75; ECF 83, at 16-17. Apellis's November 2021 Form 10-Q and February 2022 Form 10-K, for example, specifically stated that "clinical trials by their nature utilize a sample of the potential patient population," and that "with a limited number of subjects and limited duration of exposure, rare and severe side effects of [its] product candidates may only be uncovered when a significantly larger number of patients are exposed to the product." ECF 82-2, at 29; ECF 82-3, at 28; *see* ECF 81, at 8 & n.5. Such "[a]ttempts to provide investors with warnings of risks generally weaken the inference of scienter." *City of Dearborn Heights Act 345 Police & Fire Ret. Sys. v. Waters Corp.*, 632 F.3d 751, 760 (1st Cir. 2011) (quotation marks omitted).

vasculitis after the ASRS's July 2023 report as a percentage of the number of vials distributed instead of the number of patients or vials administered. *Id.* ¶¶ 132-34; *see id.* ¶¶ 141-49 (alleging other manipulations to purportedly cover up the true rate of vasculitis). These actions do not give rise to an inference, let alone a strong inference, that the defendants' prior statements about the absence of vasculitis in OAKS and DERBY were misleading *when made*. *See Ponsa-Rabell*, 35 F.4th at 33 (courts must "consider the entirety of the relevant facts available at the time of the allegedly misleading statement," with a focus on what the defendants "knew at the time"). With respect to their allegations concerning data manipulation, the plaintiffs concede that the defendants accurately disclosed that the rate was based on the number of vials distributed rather than vials administered. ECF 54, ¶ 133; *see Shash*, 84 F.4th at 17 ("The mere fact that [the defendant] engaged in post hoc analysis cannot support a strong inference of scienter where [it] did not mislead investors about the methodology employed."). And when opining as to what caused the reported incidents of vasculitis, the defendants repeatedly stated what they "believe[d]" to be true based on their findings at the time. ECF 54, ¶¶ 119-20, 124; *see* ECF 89, at 8 n.11; ECF 81, at 16-17; *Omnicare*, 575 U.S. at 187 ("A reasonable person . . . recognizes the import of words like 'I think' or 'I believe,' and grasps that they convey some lack of certainty as to the statement's content."). The plaintiffs "'may not plead fraud by hindsight,'" *id.* (quoting *ACA Fin. Guar. Corp.*, 512 F.3d at 62), by "assert[ing] no more than that because something eventually went wrong, defendants must have known about the problem earlier," *Mississippi Pub. Employees' Ret. Sys.*, 523 F.3d at 90.

In short, the plaintiffs' failure to plead sufficient facts to establish a materially misleading omission or a strong inference of scienter requires dismissal of their section 10(b) and Rule 10b-5

claim. And, without a viable underlying section 10(b) and Rule 10b-5 claim, the plaintiffs' section 20(a) claim against Dr. Francois must also be dismissed. *Zhou*, 120 F.4th at 296.

III. Leave to Amend.

Federal Rule of Civil Procedure 15(a) provides that "[t]he court should freely give leave [to amend] when justice so requires." Fed. R. Civ. P. 15(a)(2). While "[t]he rule reflects a liberal amendment policy," the Court "enjoys significant latitude in deciding whether to grant leave to amend." *ACA Fin. Guar. Corp.*, 512 F.3d at 55. Having already been afforded an opportunity to amend the complaint, the plaintiffs nonetheless request leave to file a second amended complaint should the Court grant the defendants' motion to dismiss. ECF 83, at 20 n.18; *see* ECF 48; ECF 51. The plaintiffs fail to identify, however, any additional factual allegations that they would include in a potential second amended complaint. Nor do they explain why justice otherwise requires amendment. Their request for leave to amend is, accordingly, denied. *See ACA Fin. Guar. Corp.*, 512 F.3d at 56 ("Grounds for denial include 'undue delay, bad faith or dilatory motive . . . repeated failure to cure deficiencies by amendments previously allowed, undue prejudice to the opposing party . . . [and] futility of amendment.'" (quoting *Foman v. Davis*, 371 U.S. 178, 182 (1962))); *Aponte-Torres v. Univ. of Puerto Rico*, 445 F.3d 50, 58 (1st Cir. 2006) (a plaintiff's "bare request for leave to amend," lacking a preview of "what additional facts or legal claims might be included" should amendment be allowed, "may, in and of itself, be a sufficient reason for the denial of leave to amend").

CONCLUSION AND ORDER

For the foregoing reasons, the defendants' motion to dismiss, ECF 80, is GRANTED. The amended complaint is DISMISSED with prejudice and without leave to amend.

SO ORDERED.

/s/ Julia E. Kobick
JULIA E. KOBICK
UNITED STATES DISTRICT JUDGE

Dated: March 17, 2025